

## INTERNATIONAL SEARCH REPORT

In International Application No.

PCT/EP 03/08375

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 C07K1/22 C07D401/04 C07D239/72

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>CHIJIWA T ET AL: "A NEWLY SYNTHESIZED SELECTIVE CASEIN KINASE I INHIBITOR N-2 AMINOETHYL-5-CHLOROISOQUINOLINE-8-SULFONAMIDE AND AFFINITY PURIFICATION OF CASEIN KINASE I FROM BOVINE TESTIS" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 264, no. 9, 1989, pages 4924-4927, XP002262462 ISSN: 0021-9258 abstract; page 4924, last paragraph; page 4925, paragraph joining left- and right-hand columns; page 4926, right-hand column, lines 11-25; figures 2,3; tables I,II</p> <p style="text-align: center;">----- -/--</p>	1-34

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the International filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the International filing date but later than the priority date claimed

\*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the International search

14 June 2004

Date of mailing of the International search report

26.08.04.

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

In onal Application No

PCT/EP 03/08375

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>HAYSTEAD CLARE M M ET AL:            "Gamma-Phosphate-linked ATP-sepharose for the affinity purification of protein kinases: Rapid purification to homogeneity of skeletal muscle mitogen-activated protein kinase kinase"            EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 214, no. 2, 1993, pages 459-467, XP001156617            ISSN: 0014-2956            abstract; page 462, right-hand column, second paragraph; table 1</p>	1-34
Y	<p>KNOCKAERT MARIE ET AL: "Intracellular targets of paullones: Identification following affinity purification on immobilized inhibitor"            JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 28, 12 July 2002 (2002-07-12), pages 25493-25501, XP002262473            ISSN: 0021-9258            abstract; page 25494, left-hand column, lines 49-52; page 25495, paragraph joining left- and right-hand columns; page 25496, right-hand column, lines 12-19; figures 1,2</p>	1-34
Y	<p>GALLAGHER T F ET AL: "Regulation of stress -induced cytokine production by pyridinylimidazoles; inhibition of CSBP kinase"            BIOORGANIC &amp; MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 5, no. 1, 1997, pages 49-64, XP002094123            ISSN: 0968-0896            cited in the application            abstract; figure 3; tables 2-6</p>	1-34
Y	<p>REVESZ LASZLO ET AL: "SAR of 4-hydroxypiperidine and hydroxyalkyl substituted heterocycles as novel p38 MAP kinase inhibitors"            BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 10, no. 11, 5 June 2000 (2000-06-05), pages 1261-1264, XP004200570            ISSN: 0960-894X            abstract; tables 1,2</p>	1-34

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/08375

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95/07922 A (GALLAGHER TIMOTHY F ; HEYS JOHN RICHARD (US); MCDONNELL PETER C (US) 23 March 1995 (1995-03-23) compounds on page 24; page 30, line 15 - page 31, line 2; table I; figures 6,7,9	1-34
E	WO 03/084981 A (AMBIT BIOSCIENCES CORP) 16 October 2003 (2003-10-16) examples 3,4	1-34
A	US 2001/014649 A1 (WILCHEK MEIR ET AL) 16 August 2001 (2001-08-16) abstract; page 3, right-hand column, fourth paragraph	1,3-13
A	WO 00/55185 A (BRUENING RONALD L ; IBC ADVANCED TECH INC (US); DILEO ANTHONY L (US) 21 September 2000 (2000-09-21) page 10, lines 10-18; claim 1	1,3-13
A	THULLNER SANDRA ET AL: "The protein kinase A catalytic subunit Cbeta2: Molecular characterization and distribution of the splice variant" BIOCHEMICAL JOURNAL, vol. 351, no. 1, 1 October 2000 (2000-10-01), pages 123-132, XP002283884 ISSN: 0264-6021 abstract; page 124, left-hand column, second paragraph; page 124, right-hand column, second and third paragraphs	1-34
Y	KLUTCHKO S R ET AL: "2-Substituted AMINOPYRIDO[2,3-D]PYRIMIDIN-7(8H)-ONES. STRUCTURE-ACTIVITY RELATIONSHIPS AGAINST SELECTED TYROSINE KINASES AND IN VITRO AND IN VIVO ANTICANCER ACTIVITY" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 41, no. 17, 1998, pages 3276-3292, XP002191992 ISSN: 0022-2623 abstract; tables 1-3	1-34
Y	WO 02/12238 A (WARNER LAMBERT CO ; HAMBY JAMES MARINO (US); KLUTCHKO SYLVESTER (US);) 14 February 2002 (2002-02-14) abstract; page 2, last paragraph; page 9, lines 23-28; page 10, lines 28-31; examples 8-20; table 1; claims 1-17	1-34

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## INTERNATIONAL SEARCH REPORT

In .onal Application No

PCT/EP 03/08375

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TRUMP-KALLMEYER S ET AL: "DEVELOPMENT OF A BINDING MODEL TO PROTEIN TYROSINE KINASES FOR SUBSTITUTED PYRIDOÄ2,3-DÜPYRIMIDINE INHIBITORS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 41, no. 11, 1998, pages 1752-1763, XP002164517 ISSN: 0022-2623 abstract; tables 1 and 2	1-34
Y	SCHROEDER M C ET AL: "SOLUBLE 2-SUBSTITUTED AMINOPYRIDOÄ2,3-DÜPYRIMIDIN-7-YL UREAS. STRUCTURE-ACTIVITY RELATIONSHIPS AGAINST SELECTED TYROSINE KINASES AND EXPLORATION OF IN VITRO AND IN VIVO ANTICANCER ACTIVITY" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 44, no. 12, 7 June 2001 (2001-06-07), pages 1915-1926, XP001152609 ISSN: 0022-2623 abstract; tables 1-4	1-34
Y	US 5 733 913 A (BLANKLEY CLIFTON JOHN ET AL) 31 March 1998 (1998-03-31) abstract; column 11, lines 50-54; schemes VI and X; examples 1-125	1-34
Y	MOHAMMADI MOOSA ET AL: "Crystal structure of an angiogenesis inhibitor bound to the FGF receptor tyrosine kinase domain" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 17, no. 20, 15 October 1998 (1998-10-15), pages 5896-5904, XP002283885 ISSN: 0261-4189 abstract; figure 1	1-34

# INTERNATIONAL SEARCH REPORT

national application No:  
PCT/EP 03/08375

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-34 (partially)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-34 (all partially, i.e. Inventions 1 and 2)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-34 (partially)

Independent claims 1 and 14 relate to an extremely large number of compounds in view of the broad definition of the substituents of the heterocyclic core structure and the fact that the linkage between the compound and the support material is not defined.

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty for the claimed subject-matter, even when limiting the scope of the claim only to the compounds of formula I. As the essential structural feature of formula I is simply the imidazole ring (minimal heterocyclic core structure), and any kind of linkage to the support material is to be taken into account, too many documents were retrieved (e.g. documents relating to immobilized peptides comprising an histidine residue and other immobilized imidazole moieties for affinity chromatography like WO00/55185 and US2001/0014649).

In addition, the claims relate to compounds defined by reference to a desirable characteristic or property, namely their suitability for the separation of ATP binding proteins. The claim scope covers all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds.

The claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the claimed subject-matter by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, and which relate to inventions 1 and 2, namely those parts of claims 1-34 relating to:

- i) the compounds of formulae I and IIa/b referred to in claims 2 and 15,
- ii) the pyridinylimidazoles disclosed on pages 58 and 59,
- iii) the pyrido-pyrimidine derivatives disclosed on pages 56-58, and
- iv) closely related analogues (see also the non-unity reasoning).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/08375

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WO 9507922	A	23-03-1995	US 5783664 A	21-07-1998
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Information on patent family members

In International Application No

PCT/EP 03/08375

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